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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/784,305	02/24/2004	R. Elaine Fulton	NEL-0018/NP	1520

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EXAMINER	
CHEN, STACY BROWN	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 07/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/784,305	FULTON ET AL.	
	Examiner	Art Unit	
	Stacy B. Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *1-3 and 11-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4,5 and 7-10* is/are rejected.

7)☒ Claim(s) *6* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/10/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election of Group II, claims 4-10, filed May 3, 2005 is acknowledged. Because Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 1-15 are pending. Claims 1-3 and 11-15 are withdrawn from consideration, being drawn to non-elected subject matter. Claims 4-10 are under examination.

Information Disclosure Statement

2. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 10 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which

it is most nearly connected, to make and/or use the invention. It is apparent that monoclonal antibody mA116 is required to practice the claimed invention because it is a necessary limitation for the success of the invention as stated in the claims. As a required element it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the enablement requirements of 35 U.S.C. § 112, first paragraph, may be satisfied by a deposit of mA116. See 37 CFR 1.802. Access to mA116 is required to practice the invention. The specification does not provide a repeatable method for obtaining mA116 without access to the hybridoma cell line that secretes mA116 which does not appear to be readily available material.

Deposit of mA116 in a recognized deposit facility would satisfy the enablement requirements of 35 U.S.C. 112, because the antibody would be readily available to the public to practice the invention claimed, see 37 CFR 1.801- 37 CFR 1.809.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty **and** that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating

that the deposit has been made at an acceptable depository and that the following criteria have been met:

(a) during the pendency of this application, access to the invention will be afforded to one determined by the Commissioner to be entitled thereto;

(b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

(d) a viability statement in accordance with the provisions of 37 CFR 1.807; and

(e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803 - 37 CFR 1.809 for additional explanation of these requirements.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5 and 7-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- Claim 5 recites, "[...]comprising an amino acid sequence encoded by the nucleotide sequence shown in SEQ ID NO:1". The metes and bounds of the phrase, "an amino

acid sequence", cannot be determined because the term, *an*, suggests that only a portion of the whole amino acid sequence encoded by SEQ ID NO: 1 is included in the fusion protein. If Applicant intends for at least the entire encoded polypeptide to be included in the fusion protein, then the term, *the*, is definite and clearly conveys the components of the fusion protein. Suggested language is, "[...]comprising the amino acid sequence encoded by the nucleotide sequence shown in SEQ ID NO:1". Correction and/or clarification are required to overcome this rejection.

- The terms, "high antigen-binding affinity" and "high streptavidin-binding activity", recited in claims 7-9, are indefinite. The metes and bounds of "high" activities are relative terms of degree that are subject to individual interpretation. The terms are not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Correction is required to overcome this rejection.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 4, 7 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Aubrey *et al.* (*Biol. Chem.* 2001, 382:1621-1628, "Aubrey"). The claims are drawn to a fusion protein

comprising a single chain variable fragment antibody (scFv Ab) fused with a streptavidin binding peptide (SBP) sequence. The fusion protein has a molecular weight of about 32 kilodaltons (kD). The fusion protein displays high streptavidin binding activity.

Aubrey discloses a recombinant scFv/SBP fusion protein for quantifying a particular neurotoxin protein (abstract). The molecular weight of the fusion protein is 28 kDa, thus meeting the limitation of instant claim 7, "~32 kDa". Regarding the "high" streptavidin binding activity of Aubrey's fusion protein, it is expected to have the quality of "high" binding activity. Given that Aubrey's fusion protein is constructed using the same components (according to claims 4, 7 and 9), any functions of the instantly claimed fusion protein(s) are also expected to be characteristics of Aubrey's fusion protein. Aubrey's fusion protein, illustrated in Figure 1, anticipates the instant claims.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 4 and 7-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alvi *et al.* (*Hyrbridoma and Hybridomics*, 2002, 21(3):169-178, "Alvi") in view of Keefe *et al.* (*Protein Expression and Purification*, 2001, 23:440-446, "Keefe") and Aubrey. The claims are drawn to a fusion protein comprising a single chain variable fragment antibody (scFv Ab) fused with a

streptavidin binding peptide (SBP) sequence, wherein the fusion protein displays high antigen-binding affinity to Venezuelan equine encephalitis virus (VEE).

Alvi discloses anti-VEE scFv antibodies for detecting VEE (abstract). The antibody that Alvi uses to construct the scFv antibody is the monoclonal antibody scFv 1A4A1, which is also referred to as mAb 116A (alternatively notated "mA116"). Alvi reports that the mA116 anti-VEE scFv minimally reacts with the target VEE antigen (page 178, first column). Alvi fails to teach a fusion protein comprising anti-VEE scFv fused to SBP.

However, Keefe teaches that the SBP-tag (Strep-II) is useful for purification and detection of recombinant proteins, specifically, protein, peptide and small molecule detection (abstract). Keefe also teaches that the recombinant proteins containing SBP-tags are able to be probed with a wide range of streptavidin-derivatized reagents that are commercially available, rendering the SBP-tag versatile (page 444, second column, last paragraph). Keefe also teaches that they identified a streptavidin mutant that binds the Strep-tag II with an affinity of about 1 micromolar (page 441, column 1, second full paragraph). It would have been obvious to make a fusion protein comprising Alvi's scFv antibody and Keefe's SBP-tag. One would have been motivated to make such a fusion protein because Keefe teaches that the SBP-tag is useful for detection immunoassays (abstract), and Alvi teaches that the mA116 scFv minimally reacts with its target VEE antigen. By making a fusion protein of Alvi's scFv and Keefe's SBP-tag, the result would be improved detection of VEE via improved binding between Strep-II tag and Keefe's mutant streptavidin. One would have had a reasonable expectation of success that a fusion protein would have worked in a detection assay because Aubrey's recombinant scFv/SBP fusion protein for quantifying a particular neurotoxin protein (abstract) was successful.

Therefore, the invention would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Conclusion

7. No claim is allowed. Claim 6 is objected to for depending from a rejected claim.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James C. Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Stacy B. Chen

Stacy B. Chen
July 5, 2005